Application No.: 10/556,931

Office Action Dated: December 4, 2007

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A compound according to Formula (I)

$$(R^{1})_{p}$$

$$A^{2}$$

$$A^{3}$$

$$A^{4}$$

$$A^{2}$$

$$A^{3}$$

$$A^{4}$$

$$A^{2}$$

$$A^{4}$$

$$A^{2}$$

$$A^{4}$$

$$A^{2}$$

$$A^{2}$$

$$A^{4}$$

$$A^{2}$$

$$A^{2}$$

$$A^{3}$$

$$A^{4}$$

$$A^{4}$$

$$A^{5}$$

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof, an N-oxide form thereof or a quaternary ammonium salt thereof, wherein

 $-a^1=a^2-a^3=a^4$ - is a bivalent radical of formula

N=CH CH=CH (a 1),

-CH=N-CH=CH (a 2),

-CH=CH-N=CH- (a-3) or

-CH=CH-CH=N- (a-4);

 $-Z^1$ — Z^2 - is a bivalent radical of formula

$$-O-CH_2-O-$$
 (b-1),

$$-O-CH_2-CH_2-O-$$
 (b-2),

$$-NR^{7}-CH_{2}-CH_{2}-O-$$
 (b-3),

$$-NR^7$$
-CH₂-CH₂-NR⁷ (b 5) or

wherein R⁷ is hydrogen, hydroxy, alkyl, alkyloxyalkyl or alkylcarbonyl;

X is $CR^6 \frac{}{or} N$:

each R¹, R², R³, R⁴ and R⁶ is independently hydrogen, halo, cyano, nitro, <u>or alkyl</u>, <u>alkenyl</u>, <u>mono or dialkylaminoalkyl</u>, hydroxy, <u>alkyloxy</u>, <u>alkyloxy</u>, <u>alkyloxy</u>, <u>amino</u>, <u>mono or dialkylamino</u>, <u>formylamino</u>, <u>alkylcarbonylamino</u>, <u>alkylsulfonylamino</u>, <u>hydroxycarbonyl</u>, <u>alkyloxycarbonyl</u>, <u>aminocarbonyl</u>, <u>mono or dialkylaminocarbonyl</u>, <u>alkylcarbonyloxy</u>, <u>alkylthio</u>, <u>aryl or heteroaryl</u>;

p is an integer equal to 0, 1, 2 or 3;

R⁵ is hydrogen or alkyl;

Application No.: 10/556,931

Office Action Dated: December 4, 2007

Y is a bivalent radical of formula

wherein

m is an integer equal to 0 or 1;

n is an integer equal to 0, 1, 2, 3, 4, 5 or 6;

the dotted line represents an optional double bond;

R⁸ is hydrogen, halo, alkyl, hydroxy, alkyloxy, alkylcarbonyloxy, alkyloxycarbonyl, aminocarbonyl, mono or dialkylaminocarbonyl, alkyloxycarbonyl or amino;

alkyl represents a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms; said radical being optionally substituted with at least one phenyl, halo, cyano, oxo, hydroxy, formyl or amino radical;

alkenyl represents a straight or branched unsaturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic unsaturated hydrocarbon radical having from 3 to 6 carbon atoms; said radical having at least one-double bond and said radical being optionally substituted with at least one-phenyl, halo, cyano, oxo, hydroxy, formyl or amino radical;

aryl represents phenyl or naphthyl, optionally substituted with at least one-radical that is alkyl, halo, cyano, oxo, hydroxy, alkyloxy or amino; and

heteroaryl is a monocyclic heterocyclic radical that is azetidinyl, pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl, homopiperidinyl, dioxyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, imidazolidinyl, tetrahydrofuranyl, 2H-pyrrolyl, pyrrolinyl, imidazolinyl, pyrrazolinyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, furanyl, thienyl,

Application No.: 10/556,931

Office Action Dated: December 4, 2007

oxazolyl, isoxazolyl, thiazolyl, thiadiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl or triazinyl; each radical optionally substituted with at least one-radical that is alkyl, aryl, arylalkyl, halo, cyano, oxo, hydroxy, alkyloxy or amino;

with the proviso that compounds wherein simultaneously $-a^1=a^2-a^3=a^4$ is (a-4), $-Z^1$ — Z^2 is (b-2) and Y is (c-2) are excluded.

- 2. (Canceled)
- 3. (Currently Amended) The compound according to claim 1, wherein $\mathbb{Z}^1 \mathbb{Z}^2$ is a bivalent radical of formula (b 1), (b 2) or (b 3) wherein \mathbb{R}^7 is hydrogen or methyl.
- 4. (Previously Presented) The compound according to claim 1, wherein Y is a bivalent radical of formula (c-1) wherein n = 3 and R^8 is hydrogen or of formula (c-2) wherein m = 0 or 1 and R^8 is hydrogen.
- 5. (Previously Presented) The compound according to claim 1, wherein X is CR⁶; R², R³, R⁴ and R⁶ are each independently hydrogen, halo, cyano, nitro or hydroxy; and R⁵ is hydrogen.
- 6. (Currently Amended) The compound according to claim 1, wherein $-a^4 = a^2 a^3 = a^4 is a$ bivalent radical of formula (a 3) or (a 4); $Z^1 Z^2 is$ a bivalent radical of formula (b 1), (b 2) or (b 3) wherein R^7 is hydrogen or methyl; Y is a bivalent radical of formula (c-1) wherein n = 3 and R^8 is hydrogen or (c-2) wherein m = 0 or 1 and R^8 is hydrogen; X is CR^6 ; R^2 , R^3 , R^4 and R^6 are each independently hydrogen, halo, cyano, nitro or hydroxy and R^5 is hydrogen.
- 7. (Canceled)
- 8. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and, as active ingredient, a therapeutically effective amount of a compound according to claim 1.
- 9. (Withdrawn) A method for the prevention and/or treatment in a mammal of a disorder or disease responsive to the inhibition of dopamine D₂, D₃ and/or D₄-receptors,

Application No.: 10/556,931

Office Action Dated: December 4, 2007

comprising administering to the mammal a therapeutically effective amount of a compound according to claim 1.

- 10. (Withdrawn) A method for the prevention and/or treatment in a mammal of a disorder or disease responsive to the inhibition of serotonin reuptake and antagonism of 5-HT_{1A} receptors, comprising administering to the mammal a therapeutically effective amount of a compound according to claim 1.
- 11. (Withdrawn) A method for the prevention and/or treatment in a mammal of a disorder or disease responsive to the combined effect of a dopamine D₂, D₃ and/or D₄ antagonist, a selective serotonin reuptake inhibitor (SSRI) and a 5-HT_{1A}-agonist, partial agonist or antagonist, comprising administering to the mammal a therapeutically effective amount of a compound according to claim 1.
- 12. (Withdrawn) A method for the prevention and/or treatment in a mammal of general anxiety disorder, panic disorder, obsessive compulsive disorder, depression, social phobia, eating disorders, psychosis or neurological disorders, comprising administering to the mammal a therapeutically effective amount of a compound according to claim 1.
- 13. (Withdrawn) A method for the prevention and/or treatment of schizophrenia in a mammal, comprising administering to the mammal a therapeutically effective amount of a compound according to claim 1.
- 14. (Withdrawn/Currently Amended) A process for the preparation of a compound according to Formula (I) comprising
 - --alkylating a compound-of Formula (III) with a compound of Formula (II), , in a reaction-inert solvent and optionally in the presence of a base;

$$(R^{1})_{p}$$

$$A^{2}$$

$$A^{3}$$

$$A^{4}$$

$$Z^{2}$$

$$CH_{2}-W$$

$$H-Y$$

$$R^{2}$$

$$X$$

$$R^{4}$$

$$R^{5}$$

wherein W is a leaving group; or

PATENT

DOCKET NO.: JANS-0088(PRD2059USPCT)

Application No.: 10/556,931

Office Action Dated: December 4, 2007

--reductively aminating a compound-of Formula (IV) is-with a compound-of Formula (III) in a reaction-inert solvent and in the presence of a reducing agent; or

$$(R^{1})_{p}$$

$$A^{2}$$

$$A^{3}$$

$$A^{3}$$

$$A^{4}$$

$$Z^{2}$$

$$CHO$$

$$+ H-Y$$

$$R^{5}$$

$$(IV)$$

$$(III)$$

--reacting an acid chloride of Formula (V) with a compound-of Formula (III) in a reaction-inert solvent and in the presence of a suitable base, and reducing the amide in a reaction-inert solvent in the presence of a reducing agent;

$$(R^{1})_{p}$$

$$\downarrow a^{2}$$

$$\downarrow a^{3}$$

$$\downarrow a^{3}$$

$$\downarrow a^{3}$$

$$\downarrow a^{3}$$

$$\downarrow a^{4}$$

$$\downarrow Z^{2}$$

$$\downarrow C$$

 $-a^1=a^2-a^3=a^4$ is a bivalent radical of formula

N=CH CH=CH (a 1),

-CH=N-CH=CH (a-2),

-CH=CH-N=CH- (a-3) or

-CH=CH-CH=N- (a-4);

 $-Z^1$ — Z^2 - is a bivalent radical of formula

 $-O-CH_2-O-$ (b-1),

 $-O-CH_2-CH_2-O-$ (b-2),

 $-NR^{7}-CH_{2}-CH_{2}-O-$ (b-3)

-O-CH₂-CH₂-NR⁷- (b-4).

 $-NR^7$ $-CH_2$ $-CH_2$ $-NR^7$ (b.5) or

S CH2 CH₂ O (b 6);

wherein R⁷ is hydrogen, hydroxy, alkyl, alkyloxyalkyl or alkylcarbonyl;

X is CR^6 -or N;

Page 6 of 11

Application No.: 10/556,931

Office Action Dated: December 4, 2007

each R¹, R², R³, R⁴ and R⁶ is independently hydrogen, halo, cyano, nitro, <u>or alkyl</u>, <u>alkenyl</u>, <u>mono or dialkylaminoalkyl</u>, hydroxy, <u>alkyloxy</u>, <u>alkyloxy</u>, <u>alkylcarbonyloxy</u>, <u>amino</u>, <u>mono or dialkylamino</u>, <u>formylamino</u>, <u>alkylcarbonylamino</u>, <u>alkylcarbonyl</u>, <u>alkyloxycarbonyl</u>, <u>aminocarbonyl</u>, <u>mono or dialkylaminocarbonyl</u>, <u>alkylcarbonyloxy</u>, <u>alkylthio</u>, <u>aryl or heteroaryl</u>;

p is an integer equal to 0, 1, 2 or 3;

R⁵ is hydrogen or alkyl;

Y is a bivalent radical of formula

wherein

m is an integer equal to 0 or 1;

n is an integer equal to 0, 1, 2, 3, 4, 5 or 6;

the dotted line represents an optional double bond;

R⁸ is hydrogen, halo, alkyl, hydroxy, alkyloxy, alkylcarbonyloxy, alkyloxycarbonyloxy, hydroxycarbonyl, aminocarbonyl, mono-or dialkylaminocarbonyl, alkyloxycarbonyl or amino;

alkyl represents a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms; said radical being optionally substituted with at least one phenyl, halo, cyano, oxo, hydroxy, formyl or amino radical;

alkenyl represents a straight or branched unsaturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic unsaturated hydrocarbon radical having from 3 to 6 carbon atoms; said radical having at least one-double bond and said radical being optionally substituted with at least one-phenyl, halo, cyano, oxo, hydroxy, formyl or amino radical;

Application No.: 10/556,931

Office Action Dated: December 4, 2007

aryl represents phenyl or naphthyl, optionally substituted with at least one-radical that is alkyl, halo, cyano, oxo, hydroxy, alkyloxy or amino; and heteroaryl is a monocyclic heterocyclic radical that is azetidinyl, pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl, homopiperidinyl, dioxyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, imidazolidinyl, tetrahydrofuranyl, 2H-pyrrolyl, pyrrolinyl, imidazolinyl, pyrrazolinyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiadiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl or triazinyl; each radical optionally substituted with at least one-radical that is alkyl, aryl, arylalkyl, halo, cyano, oxo, hydroxy, alkyloxy or amino.

PATENT

- 15. (Withdrawn) The process of claim 14, further comprising converting the compound of Formula (I) into a therapeutically active, non-toxic acid addition salt by treatment with an acid.
- 16. (Withdrawn) The process of claim 15, further comprising converting the acid addition salt into a free base by treatment with alkali.
- 17. (Withdrawn) The process of claim 16, further comprising converting the compound of Formula (I) into a stereochemically isomeric form, a N-oxide, or a quaternary ammonium salt.
- 18. (Withdrawn) The process of claim 14, further comprising converting the compound of Formula (I) into a therapeutically active, non-toxic base addition salt by treatment with a base.
- 19. (Withdrawn) The process of claim 18, further comprising converting the base addition salt into a free acid by treatment with an acid.